

II. REMARKS

Formal Matters

Claims 1, 3, 5, 6, 13-15, 17-21, 33, 35, 36, and 38-43 are pending.

Claims 1, 3, 5, 15, 17-21, 33, 35, 36, and 38-43 were rejected.

Applicants respectfully request reconsideration of the application in view of the remarks made herein.

Rejection withdrawn

Applicants note with gratitude that the rejection under 35 U.S.C. §112, second paragraph, as raised in the June 23, 2005 Office Action, has been withdrawn.

Rejections under 35 U.S.C. §112, first paragraph

Claims 1, 3, 5, 15, 17-21, 33, 35, 36, and 38-43 were rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enablement. Claims 1, 3, 5, 15, 17-21, 33, 35, 36, and 38-43 were rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement.

Enablement

The Advisory Action stated that the claims remain rejected for reasons of record set forth in the September 2, 2004 and April 6, 2005 Office Action.

Fatty acid desaturases

The Advisory Action stated that an artisan cannot reasonably predict whether any fatty acid desaturase from any species of mammal would necessarily have the same enzymatic activity as it has in the original animal. Applicants respectfully traverse the rejection.

The test for enablement is not whether a fatty acid desaturase from any species of mammal would necessarily have the same enzymatic activity as it has in the original animal. Instead, the test for enablement is whether those skilled in the art would find it reasonable to conclude that, given the disclosure in the specification, combined with the knowledge in the art, one of ordinary skill in the art could make and use a transgenic non-human mammal as claimed, i.e., a non-human transgenic mammal comprising a transgene comprising a nucleotide sequence encoding a fatty acid desaturase, wherein said fatty acid desaturase-encoding nucleotide sequence is operably linked to a mammary gland-specific

promoter, wherein the transgene is expressed in a mammary gland epithelial cell of said mammal, and wherein said mammal produces milk comprising a level of monounsaturated fatty acids (MUFA) that is at least 5% higher than the level of MUFA in milk produced by a non-transgenic mammal of the same species.

The specification provides ample description for how to make and use a transgenic non-human mammal comprising a desaturase-encoding transgene. The specification provides sources for nucleotide sequences encoding various desaturase proteins, which nucleotide sequences were well known in the art as of the priority date of the instant patent application. Specification, paragraph 0066. The specification provides working examples of transgenic non-human mammals comprising a transgene encoding SCD. Using the ample guidance provided in the specification, together with the knowledge and skill level in the art, those of ordinary skill in the art could make a transgenic non-human mammal comprising a transgene encoding any fatty acid desaturase.

As of the September 17, 2002 priority date of the instant application, a large number of fatty acid desaturases were known and had been characterized enzymatically; and the nucleotide sequences encoding numerous such fatty acid desaturases were known. The instant specification provides the GenBank accession numbers of several nucleotide sequences encoding various fatty acid desaturases.

In the instant application, Stearoyl CoA desaturase (SCD) was chosen as a model fatty acid desaturase, and SCD transgenic mice and goats were generated and characterized. However, one could readily generate a transgenic non-human mammal, as claimed, where the transgenic non-human mammal includes a transgene encoding any of a variety of fatty acid desaturases. For example, if a fatty acid desaturase-encoding nucleotide sequence were under transcriptional control of a mammary gland-specific promoter, one would reasonably expect that such a transgenic non-human mammal would produce milk having a level of monounsaturated fatty acids (MUFA) that is higher than the level of MUFA in milk of a non-transgenic mammal of the same species. This is because the structures of a wide variety of fatty acid desaturases are known and are conserved.

As discussed in the Declaration of James Murray, provided herewith as Exhibit 1, it is reasonable to expect that the results that were observed, using SCD as model fatty acid desaturase, would be observed using other fatty acid desaturases as transgenes. This is because the structures of a wide variety of fatty acid desaturases are known and the functional sites (e.g., catalytic domains) are

conserved. Furthermore, the ability of fatty acid desaturase genes from various eukaryotic species to function in transgenic plants or animals has been demonstrated.

The April 6, 2005 Office Action stated that the art teaches that the family of fatty acid desaturases is vast, and that an artisan cannot predict whether any fatty acid desaturase from any species of mammal would necessarily have the same enzymatic activity as it has in the original animal. However, claim 1 recites that a tissue of the transgenic non-human mammal comprises a level of MUFA that is at least 5% higher than the level of MUFA in the same tissue of a non-transgenic mammal of the same species. The specification provides ample description as to how to measure the level of MUFA in a tissue of a transgenic non-human mammal. All that would be required to determine whether a given fatty acid desaturase transgene, when expressed in a transgenic non-human mammal, resulted in a higher level of MUFA in a tissue of the mammal, would be to measure the level of MUFA in the transgenic mammal. The specification teaches how to accomplish such. Accordingly, the specification is enabling for the full scope of the claims.

The April 6, 2005 Office Action stated that an artisan cannot predict if any transgene can be expressed in any species of animal. However, the specification teaches how to determine whether a given transgene is expressed. Furthermore, those skilled in the art are well aware of various methods of determining whether a transgene is expressed. Accordingly, the specification is enabling for the full scope of the claims.

PUFAs

The Advisory Action stated that the specification has not provided any guidance as to how the claimed invention makes any PUFA. The April 6, 2005 Office Action, the Examiner stated that SCD cannot catalyze the formation of fatty acids with more than one double bond, to generate linoleic acid.

However, as discussed in the Declaration of James Murray (Exhibit 1), SCD can in fact catalyze the formation of fatty acids with more than one double bond, to linoleic acid. An example of a CLA that can be generated by the action of SCD is C18:2 *cis-9 trans-11* fatty acid, whereby rumenic acid (18:1 *trans-11*) produced by rumen bacteria is acted upon by SCD in the tissues of ruminant animals, such as dairy cattle, to produce the CLA 18:2 *cis-9 trans-11* (Griinari et al., *J. Nutr.* 130:2285-2291, 2000; Corl et al., *J. Nutr. Biochem.* 12:622-630; copies of which are provided as Exhibits 8 and 9, respectively).

The data presented in the instant application demonstrated that the level of CLA is increased in SCD transgenic goats. See, e.g., Figure 1C of the instant application.

The Advisory Action stated that conjugated linoleic acid (CLA) is not a PUFA. This is not correct. CLA is indeed a PUFA, i.e., a fatty acid with at least two carbon:carbon double bonds. For example, the CLA 18:2 *cis-9 trans-11* has an 18-carbon chain and 2 double bonds.

Promoters

The Advisory Action stated that the art teaches the unpredictability in using any heterologous promoter in any transgenic non-human mammal. However, claim 1 currently recites that the fatty acid desaturase-encoding nucleotide sequence is operably linked to a mammary gland-specific promoter. Furthermore, the September 2, 2004 Office Action appeared to indicate that the specification is enabling for a transgene operably linked to a mammary gland tissue promoter.

Methods for producing non-human transgenic mammals

The Advisory Action stated that the method of claim 18 is enabled for a method in which the non-human transgenic mammal is made by nuclear transfer.

The Advisory Action stated that the method of claim 18 is not enabled for the full scope of promoter and any fatty acid desaturase.

Applicants note that claim 18 recites a method for producing a non-human transgenic mammal according to claim 1. Claim 1 recites that the fatty acid desaturase-encoding nucleotide sequence is operably linked to a mammary gland-specific promoter. As noted above, the September 2, 2004 Office Action appeared to indicate that the specification is enabling for a transgene operably linked to a mammary gland tissue promoter. Furthermore, as discussed above, it is Applicants' position that the instant specification is enabling for a transgenic non-human mammal comprising a transgene encoding a fatty acid desaturase, as recited in the instant claims.

Written description

The Advisory Action stated that the specification does not provide any guidance to the artisan to obtain any fatty acid desaturase because the genus encompasses a large number of species that would have different structures. The Advisory Action stated that the claims are broad for any tissue-specific promoter.

Fatty acid desaturase

The written description requirement of 35 U.S.C. §112, first paragraph, requires that Applicants describe the invention in such a way that those skilled in the art would recognize that Applicants were in possession of the invention as claimed, as of the priority date. MPEP §2163 states that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species; and that a “representative number of species” means that the species which are adequately described are representative of the entire genus. MPEP §2163 states that there may be situations in which one species adequately supports a genus; and that what constitutes a “representative number” is an inverse function of the skill and knowledge in the art.

Those skilled in the art would recognize that, as of the priority date of the instant application, Applicants had possession of the instant invention as claimed. As noted previously, the specification discloses publicly available sources of nucleotide sequences encoding a variety of fatty acid desaturases, as well as a variety of stearoyl CoA desaturases. Accordingly, those skilled in the art would recognize that Applicants had possession of the invention as claimed. Accordingly, the specification provides adequate written description of fatty acid desaturase transgenes, and transgenic non-human mammals comprising same.

As discussed in the Declaration of James Murray (Exhibit 1), the function of fatty acid desaturases is conserved. Thus, given the disclosure of the instant application in combination with the knowledge and skill level in the art, those skilled in the art would recognize that, as of the priority date of the instant application, Applicants had possession of the instant invention as claimed.

The Federal Circuit’s decision in *Capon v. Eshhar* (Fed. Cir. No. 03-1480, August 12, 2005; “*Capon*”) (Exhibit 10) is relevant to the instant case. *Capon* involved an interference between two parties claiming a chimeric DNA encoding a chimeric single-chain antibody. The parties argued that there was no need to know the structure of the DNA segments to make the claimed chimeric DNAs, because the structure of these components were already known, and methods for identifying, obtaining, and linking DNA segments were known. Despite this showing, the Board of Patent Appeals and Interferences (the “Board”) found that neither party’s specification met the written description requirement of 35 U.S.C. §112, first paragraph. The Board stated that:

Their specifications do not satisfy the written description requirement because persons having ordinary skill in the art would not have been able to visualize and recognize the identity of the claimed genetic materials without considering additional knowledge in the art, performing additional experimentation, and testing to confirm results.¹

The Federal Circuit reversed, finding that the Board “erred in refusing to consider the state of the scientific knowledge”.² The court in *Capon* stated:

The Board’s rule that the nucleotide sequences of the chimeric genes must be fully presented, although the nucleotide sequences of the component DNA are known, is an inappropriate generalization. When the prior art includes the nucleotide information, precedent does not set a *per se* rule that the information must be determined afresh.³

and

The “written description” requirement states that the patentee must describe the invention; it does not state that every invention must be described in the same way. As each field evolves, the balance also evolves between what is known and what is added by each inventive contribution... The chimeric genes here at issue are prepared from known DNA sequences of known function....The Board erred in holding that the specifications do not meet the written description requirement because they do not reiterate the structure or formula or chemical name for the nucleotide sequences of the claimed chimeric genes.⁴

The Advisory Action and the previous Office Actions raise issues similar to those raised by the Board and addressed by the Federal Circuit in *Capon*. The claimed invention encompasses use of materials that were available in the art -- various nucleic acids encoding fatty acid desaturases -- to produce transgenic non-human mammals using known methods. The claimed invention is directed to a non-human transgenic mammal comprising a fatty acid-encoding transgene. Accordingly, as in *Capon*, the Office should find that Applicants’ specification fulfills the written description requirement under §112, first paragraph with respect to the claimed invention.

In *Capon*, the Federal Circuit noted that in *Lilly*, which involved claims to a vertebrate cDNA encoding insulin, the cDNA for human insulin *had never been characterized*. This was not the case in

¹ *Capon* at page 9 (citing Board opinion).

² *Capon* at page 14.

³ *Capon* at page 15.

⁴ *Capon* at page 15.

Capon, in which there was ample information available in the art. Just as in *Capon*, the present invention does **not** involve the situation in *Lilly*, which involved claims to a novel gene. In short, the *Lilly* decision simply does not apply to the instant case. Instead, the facts of *Capon* are more similar to those of the instant case. Accordingly, the Office should find, as did the Federal Circuit in *Capon*, that the specification satisfies the written description requirement of 35 U.S.C. §112, first paragraph for the claimed invention.

Promoters

The Advisory Action stated that the claims are broad for any tissue-specific promoter. However, as noted above, claim 1 recites that the fatty acid desaturase-encoding nucleotide sequence is operably linked to a **mammary gland-specific** promoter.

As discussed previously, the instant application provides a number of mammary gland-specific promoters. Furthermore, as of the priority date of the instant application, a number of mammary gland-specific promoters were known in the art. Just as the Federal Circuit found in *Capon*, the Office should find that the instant claims meet the written description requirement.

Conclusion as to the rejections under 35 U.S.C. §112, first paragraph

Applicants submit that the rejections of claims 1, 3, 5, 15, 17-21, 33, 35, 36, and 38-43 under 35 U.S.C. §112, first paragraph, have been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejections.

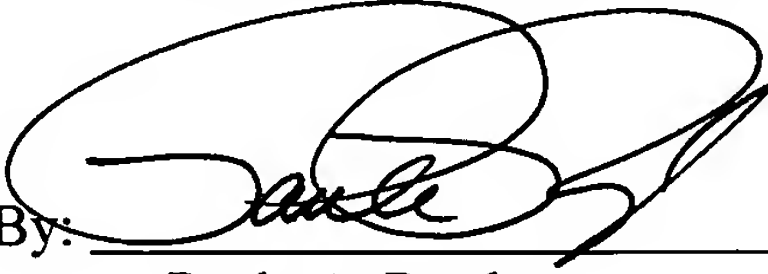
III. CONCLUSION

Applicants submit that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number UCDV-286.

Respectfully submitted,
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Date: Dec. 1, 2005

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